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# **Cortical thinning and neuropsychological changes in presymptomatic Huntington's Disease**

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degree of Doctorate of Clinical Psychology, University of Auckland, 2009.**

## Abstract

Degeneration of the striatum and striatal-frontal circuits are generally thought to cause most of the neuropsychological symptoms experienced in Huntington's Disease (HD). Advances in cortical thickness mapping (an automated MRI method for precisely measuring the cortical thickness across the entire cortex) provide a new technique for examining changes in the brain in HD. Recent studies using this technology have reported provocative results. They found significant cortical thinning in participants with early HD (Rosas et al., 2002; Rosas et al., 2008) and even in presymptomatic HD (Rosas et al., 2005). Moreover, cortical thinning was most prominent in posterior regions of the brain, with relative preservation of the anterior frontal regions. The present study replicated Rosas et al.'s (2005) study but used a larger sample of presymptomatic HD participants (n = 19) and a control group matched for age, gender and education (n = 19). Presymptomatic HD participants were divided into two groups, PreHDclose and PreHDfar, based on their estimated proximity to clinical onset. The distribution of cortical thinning was assessed using an identical MRI method to previous cortical thinning studies with HD participants. Specific neuropsychological tests were used to assess cognitive and mood changes that may be associated with cortical thinning. It was hypothesised that cortical thinning would be more evident in posterior than frontal cortical regions. It was also hypothesised that presymptomatic HD participants would perform more poorly than controls on tests that are subserved primarily by specific posterior cortical regions, but not on tests that are subserved by anterior cortical regions. Lastly, it was predicted that poorer performance in the neuropsychological measures would be associated with greater thinning in cortical regions that are important during performance of these tasks.

Consistent with predictions, the presymptomatic HD group showed regionally-specific cortical thinning which was most prominent in the posterior cortices, particularly around the right parieto-temporal-occipital (PTO) junction. Thinning occurred in people up to 15 years before clinical onset, with little to no thinning before that. The presymptomatic HD group, and particularly the PreHDclose participants, performed significantly worse than controls in 2 of the 6 cognitive tests that are subserved primarily by posterior cortical regions (the Judgment of Line

Orientation test and modified Roadmap Test), but not in tests that are subserved primarily by frontal cortical regions. Correlational analyses showed a number of regionally-specific relationships between thinning and cognitive performance, although the distribution of these relationships did not generally support our region-of-interest predictions. The results contribute to a better characterisation of the cortical and neuropsychological changes that occur early in the development of HD, and provide tentative support for cortical thickness mapping as a valid and sensitive measure for assessing cortical changes in presymptomatic HD.

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# Table of Contents

<b>Abstract</b>	<b>ii</b>
<b>Acknowledgements</b>	<b>iv</b>
<b>Table of Contents</b>	<b>vi</b>
<b>List of Tables</b>	<b>x</b>
<b>List of Figures</b>	<b>xi</b>
<b>List of Appendices</b>	<b>xv</b>
<b>List of Abbreviations</b>	<b>xvi</b>
<b>Preface</b>	<b>1</b>
<b>Chapter One Literature Review</b>	<b>2</b>
General Introduction .....	2
Background information on HD .....	3
Prevalence of HD .....	3
Genetics of HD .....	3
Neuropathology of HD .....	4
Diagnosis and prognosis of HD .....	7
Structural neuroimaging in HD.....	8
Subcortical changes in HD.....	9
Cortical changes in HD.....	12
Neuropsychological changes in HD.....	21
Psychomotor abilities.....	21
Attention .....	22
Executive functioning.....	23

Memory.....	28
Visuospatial abilities.....	30
Language abilities.....	34
Mood and personality changes.....	35
Relationships between structural MRI and clinical measures in HD.....	37
Relationship between brain changes and motor symptoms.....	37
Relationship between brain changes and the Total Functional Capacity Scale.....	38
Relationship between brain changes and cognitive performance.....	39
Present study.....	44
<b>Chapter Two      General method</b>	<b>46</b>
Participants.....	46
Screening tests.....	49
General Procedure.....	50
<b>Chapter Three      Study 1: Cortical thinning in presymptomatic HD</b>	<b>51</b>
Methods.....	52
Materials.....	52
Procedure.....	54
Statistical analysis.....	54
Results.....	58
Surface-based analyses.....	58
Cortical parcellations analyses.....	61
Striatal volume analyses.....	61
Discussion.....	62
<b>Chapter Four      Study 2: Neuropsychological changes in presymptomatic HD</b>	<b>70</b>
Introduction.....	70

Methods.....	71
Materials and procedure.....	71
Psychomotor speed tasks .....	73
Cognitive tasks sensitive to posterior cortical regions.....	73
Cognitive tasks sensitive to anterior cortical regions .....	81
Mood Assessments.....	87
Procedure of the testing session.....	88
Statistical Analysis.....	90
Results.....	91
Comparisons between total PreHD and Control groups.....	91
Comparisons between PreHDclose, PreHDfar and Control groups .....	106
Discussion.....	123
<b>Chapter Five Study 3: Clinical correlates of brain measures</b>	<b>128</b>
Introduction.....	128
Method .....	129
Statistical analysis.....	129
Results.....	132
Surface-based regressions.....	132
Correlations between cortical parcellations and neuropsychological test scores .....	137
Correlations between striatal volume and neuropsychological tests scores .....	138
Discussion.....	140
<b>Chapter Six General Discussion</b>	<b>147</b>
Summary of findings.....	147
Understanding correlations between cortical thinning and neuropsychological scores .....	149
Complexity of brain processes in presymptomatic HD .....	149

Cortical thinning and neuropsychological performance in the normal population.....	150
Poorer neuropsychological performance is associated with both thinner and thicker cortex .....	151
A priori selection of neuropsychological tasks .....	153
Basal ganglia and neuropsychological performance.....	154
Validity of the proximity to onset model .....	155
Contributions to scientific research and implications for clinical trials .....	156
Reflections on an international collaboration .....	158
Conclusions.....	159
<b>List of Appendices</b>	<b>160</b>
<b>List of references</b>	<b>185</b>

## List of Tables

Table 1: Clinical characteristics of the PreHD group .....	47
Table 2: Demographic characteristics for the PreHD and Control Groups .....	48
Table 3: Demographic characteristics for the PreHDfar, PreHDclose and Control groups .....	49
Table 4: Average cortical thinning and intracranial volumes .....	57
Table 5: Properties of neuropsychological tests selected for this study .....	72
Table 6: Mean response times and standard deviations on the motor screening and simple reaction time tasks for the PreHD and Control groups .....	91
Table 7: Mean accuracy scores, standard deviations and ranges for four tasks sensitive to posterior cortical regions: the Judgment of Line Orientation task, Hooper Visual Organisation Test; Collision Judgment task and Facial Recognition Test.....	92
Table 8: Accuracy and response times on the Roadmap Test for the PreHD group and the Control group. ....	93
Table 9: Means and standard deviations for PreHD and Control groups on the four mood assessments.....	106
Table 10: Means response times and standard deviations on the motor screening and simple reaction time task for the PreHDclose, PreHDfar and Control groups. ....	107
Table 11: Mean accuracy, standard deviation and range for the PreHDclose, PreHDfar and Control groups on four tasks sensitive to posterior cortical regions .....	107
Table 12: Accuracy and response times on the Roadmap Test for the PreHDclose, PreHDfar and Control groups. ....	109
Table 13: Performance measures for the Iowa gambling task .....	117
Table 14: Means and standard deviations on four mood assessments for the PreHDclose, PreHDfar and Control groups.....	122
Table 15: Cortical parcellation regions of interest (ROIs) associated with cognitive test measures. ....	131
Table 16: Cortical regions considered crucial to mediating cognitive task in the study .....	177

## List of Figures

<i>Figure 1:</i> Basal-ganglia thalamo-cortical circuits from Alexander, DeLong & Strick (1986).....	6
<i>Figure 2:</i> Mean cortical thickness maps from Rosas et al. (2002). .....	18
<i>Figure 3:</i> Mean cortical thickness maps from Rosas et al. (2008) .....	19
<i>Figure 4:</i> Mean cortical thickness maps from Rosas et al. (2005). .....	20
<i>Figure 5:</i> Confidence rating of Huntington disease motor abnormalities (item 17 of Unified Huntington’s Disease Rating Scale, 1998). .....	47
<i>Figure 6:</i> Image of a reconstructed MRI dataset from Fischl et al., (2008) .....	53
<i>Figure 7:</i> Lateral views of the pial surface and inflated cortical surface representations for a single participant. ....	53
<i>Figure 8:</i> 68 Cortical parcellations, shown on a normal view of the brain and an inflated view.....	56
<i>Figure 9:</i> The topology of cortical thinning in the PreHD group (n = 19) compared to the matched control group (n = 19). .....	59
<i>Figure 10:</i> The topology of cortical thinning in the PreHDclose and PreHDfar groups .....	60
<i>Figure 11:</i> Volume measures of the striatal regions in the PreHDclose, PreHDfar and Control groups.....	62
<i>Figure 12:</i> Judgment of Line Orientation Test. Participants were required to identify which of the eleven exemplar lines are the same orientation as the two stimulus lines. ....	74
<i>Figure 13:</i> Item 22 (a mouse) from the Hooper Visual Organisation Test.....	75
<i>Figure 14:</i> Collision Judgment task.....	76
<i>Figure 15:</i> Facial Recognition Test. ....	77
<i>Figure 16:</i> Modified version of the Roadmap Test of Directional Sense.....	79
<i>Figure 17:</i> Letter mental rotation task stimuli including normal and mirror image ‘F’s in all six orientations. ....	81
<i>Figure 18:</i> The Iowa Gambling Task.....	83
<i>Figure 19:</i> The Stockings of Cambridge task.....	85
<i>Figure 20:</i> Hand Rotation Task stimuli including left and right hands in all six orientations. ....	87

<i>Figure 21:</i> Mean response times for letter mental rotation task for the PreHD group and the Control group. ....	95
<i>Figure 22:</i> Mean response times for the Mirror and Normal conditions of the letter mental rotation task for the PreHD group and the Control group.....	96
<i>Figure 23:</i> Mean accuracy for letter mental rotation task for the PreHD group and the Control group.....	97
<i>Figure 24:</i> Mean response time for hand mental rotation task for the PreHD group and the Control group. ....	98
<i>Figure 25:</i> Mean accuracy for hand mental rotation task for the PreHD group and the Control group. ....	99
<i>Figure 26:</i> Mean percent correct (advantageous card selections from deck C and D) across the five time-blocks of the Iowa Gambling task for the PreHD group and the Control group.....	100
<i>Figure 27:</i> Mean proportion of perfect moves and mean number of excess moves to completion across the four problem difficulty levels of the Stockings of Cambridge task for the PreHD group and the Control group. ....	102
<i>Figure 28:</i> Mean initial thinking time and subsequent thinking time across the four problem difficulty levels of the Stockings of Cambridge task for the PreHD group and the Control group .....	103
<i>Figure 29:</i> Motor initiation times and motor execution times in the Stockings of Cambridge task for difficulty levels 2-5 for the PreHD group and the Control group .....	104
<i>Figure 30:</i> Mean percentage of correct turns for the no rotation (NR) and the rotation turns (HR and FR combined) of the Roadmap Test for the PreHDclose, PreHDfar and Control groups.....	109
<i>Figure 31:</i> Mean response times for (a) total letter mental rotation task, (b) mirror condition, and (c) normal condition, for the PreHDclose, PreHD far and Control groups.....	111
<i>Figure 32:</i> Mean accuracy for letter mental rotation task for the PreHDclose, PreHD far and Control groups.....	112

<i>Figure 33:</i> Mean accuracy for the mirror and normal conditions of the letter mental rotation task for the PreHDclose, PreHD far and Control groups .....	113
<i>Figure 34:</i> Mean response times for Hand mental rotation task for the PreHDclose, PreHD far and Control groups. ....	114
<i>Figure 35:</i> Mean response times for the left and right hand stimuli of the hand mental rotation task for the PreHDclose, PreHD far and Control group .....	114
<i>Figure 36:</i> Mean accuracy for hand mental rotation task for the PreHDclose, PreHD far and Control groups.....	116
<i>Figure 37:</i> Mean percent of advantageous card selections (from Deck C and D) across the five time-blocks of the Iowa Gambling task for the PreHDclose, PreHDfar and Control groups.....	117
<i>Figure 38:</i> Mean proportion of perfect moves and excess moves for difficulty levels 2-5 of the Stockings of Cambridge task for the PreHD group and the Control group. ....	118
<i>Figure 39:</i> Mean initial thinking time and subsequent thinking time across for difficulty levels 2-5 of the Stocking of Cambridge task for the PreHDclose, PreHDfar and Control groups.....	120
<i>Figure 40:</i> Mean motor initiation times and motor execution times in the Stockings of Cambridge task for difficulty levels 2-5 for the PreHD group and the Control group. ....	121
<i>Figure 41:</i> Significant correlations between JLOT total accuracy scores and selective cortical thinning in the PreHD group. ....	132
<i>Figure 42:</i> Significant correlations between Roadmap accuracy scores (rotation turns only) and selective cortical thinning in the PreHD group .....	133
<i>Figure 43:</i> Significant correlations between Stockings of Cambridge task (proportion of perfect solutions) and selective cortical thinning in the PreHD group .....	134
<i>Figure 44:</i> Scatter plot illustrating the correlation between performance on the Stockings of Cambridge task and a manually selected ROI within the right Pars Triangularis ...	134
<i>Figure 45:</i> Significant correlations between Iowa Gambling task (percentage of advantageous cards in last 60 trials) and selective cortical thinning in the PreHD group .....	135

<i>Figure 46:</i> Significant correlations between Outward Irritability Scale total scores and selective cortical thinning in the PreHD group.....	136
<i>Figure 47:</i> Scatter plot illustrating the correlation between performance on the Outward Irritability Scale and an ROI within the right anterior cingulate cortex .....	136
<i>Figure 48:</i> Scatter plot illustrating the positive correlation between Iowa Gambling task accuracy scores (percentage of advantageous cards in last 60 trials) and cortical thickness in the left pars opercula. ....	138
<i>Figure 49:</i> Scatter plot illustrating the positive correlation between caudate volume and Roadmap accuracy scores for the PreHD group. ....	139
<i>Figure 50:</i> Scatter plots illustrating the positive correlation between putamen volume and JLOT accuracy scores (top) and Roadmap accuracy scores (bottom) for the PreHD group. ....	139

## List of Appendices

Appendix A: UHDRS motor scale.....	161
Appendix B: Study consent form.....	164
Appendix C: MRI safety and consent form .....	165
Appendix D: Mean thicknesses of the cortical parcellations in the PreHD and Control groups .....	167
Appendix E: Mean thicknesses of the cortical parcellations in the PreHDclose, PreHDFar and Control groups .....	169
Appendix F: Rationale for cognitive tests used in this study.....	171
Appendix G: Standardised instructions for the Iowa Gambling Test.....	178
Appendix H: Hospital Anxiety and Depression Scale .....	179
Appendix I: Irritability-Depression-Anxiety Scale (IDAS).....	180
Appendix J: Structured interview .....	181
Appendix K: Correlations between cognitive test scores and mean thicknesses in the cortical parcellation regions of interest in the PreHD and Control groups .....	183

## List of Abbreviations

AD	Alzheimer's Disease
ANOVA	Analysis of Variance
BA	Brodman Area
CVLT	Californian Verbal Learning Test
DLPFC	Dorsolateral prefrontal cortex
DRS	Dementia Rating Scale
fMRI	Functional Magnetic Resonance Imaging
HADS	Hospital Anxiety and Depression Scale
HD	Huntington's Disease
HVLT	Hopkins Verbal Learning Test
HVOT	Hooper Visual Organisation Test
ICV	Intracranial volume
IDAS	Irritability-Depression-Anxiety Scale
IGT	Iowa Gambling Test
JLOT	Judgement of Line Orientation Test
MMSE	Mini-Mental State Examination
MRI	Magnetic Resonance Imaging
PET	Positron Emission Tomography
QNE	Quantified Neurological Examination
ROI	Region-of-interest
SDMT	Symbol Digit Modalities Test
SoC	Stockings of Cambridge task
TBI	Traumatic Brain Injury
TFC	Total Functional Capacity Scale
ToL	Tower of London task
UHDRS	Unified Huntington's Disease Rating Scale
VBM	Voxel-Based Morphometry
VLPFC	Ventrolateral prefrontal cortex

WCST	Wisconsin Card Sorting Test
WMS	Wechsler Memory Scale
YTO	Estimated Years To clinical Onset